REMARKS

Claims 1-13, 15-22, 38, 41 and 45-49 are rejected under 35 USC § 101 because the claimed invention is not supported by a specific asserted utility or well-established utility. The Examiner states that the specification teaches general utility for the invention, not a specific utility. These claims have been canceled.

Furthermore, Applicant respectfully disagrees. The specification teaches that the claimed sequences express themselves more abundantly in breast tissue than any other tissue, thereby establishing that breast tissue is the host tissue of the claimed gene products.

Several assays utilizing the overexpression of tissue-specific gene products have been established in the art. The court has consistently stated that claim language must be read in light of prior art and teachings of the specification. The standard is that the "definiteness of the language must be analyzed...in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art." *In re Moore*, 439 F.2d 1232, 169 USPQ 236 (CCPA 1971).

Applicant has previously described how gene products that are expressed in a host tissue but not in other tissue can be used to indicate disease when they are found to be overexpressed in tissue outside their host tissue (e.g., CEA, PSA). The polynucleotides are of interest when they are overexpressed in a tissue or body compartment where their normal occurrence is very low or non-existent (for example, the appearance of BS274 in non-breast tissue is at very low levels). Such overexpression indicates that a disease has altered the polynucleotides so that they escape from their host tissue (in this case breast tissue) into other areas of the body, such as blood. These examples demonstrate that presence of the claimed gene products outside normal host tissue serves as a diagnostic indicator that the host tissue is in a diseased state. Thus, the correlation between disease states and tissue-specific gene products, such as those claimed in the present invention, are established in the art. Because the claims should be analyzed in light of the teachings of the prior art and well-known techniques of immunohistochemistry for assessing overexpression are incorporated into the specification, Applicant asserts that the examples and methods disclosed in the specification are useful for detecting, at the least, breast diseases that may be detected using gene markers and related gene marker technology. Applicant respectfully

submits that the new claims are in a condition for allowance and requests that this rejection be withdrawn.

Applicant further reminds the Examiner that a protein or nucleic acid marker is useful not only for the direct detection of cancer in a biopsy sample but may also be useful in making a diagnosis or prognosis regarding the patient's disease status. Further, a protein or nucleic acid may not be present in high levels or at all in every tumor. For example, in the case of HER2-neu, only 1/3 of breast cancers overexpress this protein. Thus, in a breast cancer library, a very low level of HER2-neu will be present even though it is a very accurate breast cancer marker. Indeed, HER2-neu is used as a standard breast cancer marker.

Overexpression can be assessed by the well-known technique of immunohistochemistry using an antibody directed against the protein. For breast cancer patients with overexpression of HER-2-neu, treatment with Herceptin, a human-mouse chimeric antibody directed against the protein has therapeutic value. Also, if the gene which codes for HER-2-neu is amplified (multiple copies are present) as detected by the well known techniques of *in situ* hybridization, again the patient will likely respond to Herceptin treatment. However, if the patient does not exhibit an amplified gene or overexpression of the protein, treatment with Herceptin is unlikely to be of benefit.

Similarly, testing for estrogen receptor protein by immunohistochemistry is used as an indicator for treatment with anti-estrogens such as Tamoxifen. Only 2/3 of breast cancer patients express estrogen receptor in their tumors and thus benefit from Tamoxifen therapy. Based on the above, it is clear that the presence or absence of gene products, which are expressed in the body, is of diagnostic significance for cancer in a manner consistent with the methods and products claimed in new claims 52-78. Thus, the claimed polynucleotides of the present invention exhibit credible utility for several genres of tests well known in the art, whether direct or indirect in nature. Applicant respectfully submits that the new claims are in a condition for allowance and requests that this rejection be withdrawn.

Claims 1-13, 15-22, 38, 41 and 45-49 are rejected under 35 USC § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. These claims have been canceled. Moreover, Applicant asserts that in light of the above amendments and remarks, the new claims are in a condition for allowance and requests that this rejection be withdrawn.

The Examiner states that "a skilled artisan could not be expected to identity or make the polynucleotides encompassed by the instant claims. Furthermore, Applicant respectfully disagrees. Several methods are established in the art and cited in the specification for envisioning the detailed structure within the context of percent identity variants. However, in an effort to expedite prosecution, these claims have been canceled. New claims 52-78 do not contain "percent identity" language. Furthermore, new claims 52-78 encompass "complete complements and degenerate coding sequences thereof". The degeneracy of the genetic code is a concept that is well-known to those skilled in the art and is even discussed in section 2144.09 of the February 2000 revision of the Manual for Patent Examining Procedure as "the fact that most amino acids are specified by more than one nucleotide sequence or codon." Applicant respectfully submits that the new claims are in a condition for allowance and requests that this rejection be withdrawn.

The Examiner states that the term "BS274" is not an art recognized term. Applicant respectfully directs the Examiner to page 9, line 8 of the specification, which clearly defines "BS274" as a designation for a gene. Applicant respectfully reminds Examiner that an applicant is entitled to be his or her own lexicographer, and in many instances will provide an explicit definition for certain terms used in the claims. Where an explicit definition is provided by the applicant for a term, for example at page 9, line 8 of the instant specification, that definition will control interpretation of the term as it is used in the claim. However, in an effort to expedite prosecution, claims 1-13, 15-22, 38, 41 and 45-49 have been canceled and new claims 52-78 do not include "BS274" language. Applicant respectfully submits that the new claims are in a condition for allowance and requests that this rejection be withdrawn.

Claims 1-13, 15-22, 38, 41 and 45-49 are rejected under 35 USC § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. The Examiner states that the specification teaches polynucleotides consisting of SEQ ID NOS:1-7 but there is not adequate description of the genus of polynucleotides that have least 90% identity with SEQ ID NOS:1-7. In light of the above amendments, which remove "percent identity" language, Applicant respectfully submits that the new claims are in a condition for allowance and requests that this rejection be withdrawn.

CONCLUSION

In view of the aforementioned amendments and remarks, Applicant respectfully submits that the above-referenced application is now in a condition for allowance and Applicant respectfully requests that the Examiner withdraw all outstanding objections and rejections and passes the application to allowance.

Date: **JULY 16, 2001**

Respectfully submitted,
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